isolated innervated jejunum preparation (Finkleman, 1930), the drugs had the same relative order of potency in inhibiting the pendular movement induced by periaterial nerve stimulation.

The order of potency of the drugs in inhibiting the electrically induced twitches of the rat vas deferens was guanethidine > bretylium > pronethalol > propranolol > procaine. On the other hand, the order of local anaesthetic potency of the drugs is known to be propranolol > pronethalol > procaine > bretylium > guanethidine (Morales-Aguilerá & Vaughan Williams, 1965; Gill & Vaughan Williams, 1964; Papp & Vaughan Williams, 1969; Davis, 1970; Bein, 1960). There was thus no correlation of local anaesthetic and motor transmission blocking activities, since guanethidine and bretylium, the least potent local anaesthetics, were the most potent inhibitors of responses to electrical stimulation. It does not seem reasonable, therefore, to attribute the blockade of the electrically induced twitches of the vas by the adrenergic neuron blocking agents directly to their trivial local anaesthetic action.

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Effect of reserpine on catechol-*O*-methyl transferase in rat submaxillary gland

Marsden, Broch & Guldberg (1971) showed that ligation of the excretory duct of the rat submaxillary gland, which induces an atrophy of the glandular acini without affecting the adrenergic nerves, reduced the activity of the catechol-*O*-methyl transferase (COMT) in the gland by 60%, while removal of the superior cervical ganglion reduced the COMT activity by 40%. Moreover, reserpine (5 mg kg^{-1}) was found to reduce the COMT activity of unoperated glands by up to 50% at 6 and 18 h after its administration. The effects observed were thought to be due to COMT being localized extraneuronally and being dependent on the presence of the substrate (noradrenaline) for full activity.

I have now assessed the effect of reserpine on the enzyme in ganglionectomized glands. Twenty Wistar rats of either sex, 200–250 g, were treated as described by Marsden & others (1971). The left superior cervical ganglion of 10 rats was removed, atrophy was induced in the other 10 rats by ligating the excretory duct on the left side. The right gland always served as control. The animals were then left for 14 days.

Table 1. *Catechol-O-methyl transferase activity in the salivary gland after sympathectomy or ligation of the excretory duct: effect of reserpine 5 mg kg^{-1} s.c. Activities in μmol g^{-1} h^{-1}, mean of 5 experiments ± s.e.*

	No treatment	Reserpine treatment	% reduction
	Sympathectomy		
Control gland	0·43 ± 0·023	0·37 ± 0·028	14 ± 6·0
Operated gland	0·43 ± 0·032	0·44 ± 0·034	−3 ± 9·0
Operated gland, corrected*	0·39 ± 0·023	0·34 ± 0·013	13 ± 4·5**
	Ligation of excretory duct		
Control gland	0·43 ± 0·021	0·34 ± 0·025	21 ± 4·2**
Operated gland	0·79 ± 0·088	0·63 ± 0·066	20 ± 4·4**
Operated gland, corrected*	0·25 ± 0·021	0·18 ± 0·011	28 ± 6·7**
	All unoperated glands (10 of each)		
	0·43 ± 0·015	0·35 ± 0·018***	18

* Activity per g original tissue $\left(\text{Act.} \times \frac{\text{W of operated gl.}}{\text{W of control gl.}} \right)$

** Significantly different from zero ($P < 0·05$).
*** Significantly different from nontreated ($P < 0·01$).

Reserpine (Serpasil, Ciba) (5 mg kg^{-1}) was given subcutaneously to five of the rats in each group 18 h before they were killed. The animals were housed at a room temperature of 25° after the reserpine treatment.

The glands from one animal in each group were analysed at the same time to obtain paired comparisons. COMT determinations were done according to Broch (1973) in an incubation volume of 0·5 ml.

Sympathectomy gave a weight reduction of 10% (control 253; operated 227 mg ≡ 90 ± 3% n = 5) and atrophy a reduction of 70% (control 263; ligated 86 mg ≡ 33 ± 4% n = 5) in the animals not given reserpine. The differences in weight between the sympathectomized and the control glands were just significantly larger in the reserpine-treated animals (control 258; operated 199 mg ≡ 77 ± 2·5% n = 5) than in the untreated ones ($P<0·02$). Corresponding differences were not significant in the rats with atrophied glands (reserpine-treated control 228; ligated 65 mg ≡ 29 ± 1·5%). The reason for this discrepancy may be that the blood vessels of the sympathectomized glands had lost their adrenergic tone and thus were in a state of constant vasodilatation with consequently larger blood volume. This increase partly counteracted the weight reduction from the sympathectomy. In the reserpine-treated animals both glands were equally deprived of sympathetic tone.

Sympathectomy induced a reduction in the COMT activity of the whole gland of 13% ± 3·6 and ligation of the excretory duct a reduction of 42% ± 4·4 (means ± s.e.). This is less than the figures of 40 and 60% found before (Marsden & others, 1971) but the reductions were both significant ($P <0·01$).

In the control glands, reserpine caused a reduction in the COMT activity of 18% (Table 1). This was significant but much smaller than found by Marsden & others (1971). In atrophied glands, the COMT was reduced by reserpine to the same extent as in the control glands. The sympathectomized glands showed no difference in the COMT activity per weight after reserpine treatment. However, after corrections of the values for the weight loss by multiplying with the ratios (means 90% for non-treated and 77% for reserpine-treated glands) between operated and control glands the changes induced by reserpine were identical in the sympathectomized and the control gland.

The results, as well as confirming earlier findings that COMT in the rat salivary gland is reduced after ligation, sympathectomy and reserpine treatment, show that

the reductions after sympathectomy and after reserpine treatment are completely independent. Thus it is more likely that COMT exists both intraneuronally and extraneuronally and that its depression after reserpine is not mediated by substrate depletion (Marsden & others, 1971).

There are indications for the existence of two forms of COMT in the rat salivary gland, one form appears to be connected with the atrophied gland and the other with the sympathectomized one (Broch, unpublished).

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Inhibition of a minor pathway of L-dopa metabolism in the intestinal lumen using a decarboxylase inhibitor (Ro 4-4602)

The evidence for the existence of a minor pathway of L-dopa metabolism through the action of the intestinal microflora has been reviewed recently (Bakke, 1973). After the introduction of decarboxylase inhibitors in the treatment of parkinsonism to reduce the extracerebral conversion of orally administered L-dopa to dopamine, the question has arisen whether the metabolism in the intestinal lumen is also affected by such inhibitors. We have carried out experiments with cultures of intestinal microorganisms and with rats to study the effect of a decarboxylase inhibitor Ro 4-4602 (Benserazid, F. Hoffman-La Roche & Co., Switzerland) on the microbial metabolism of L-dopa and some related phenolic acids.

The methods used to study the metabolism in anaerobic cultures of mixed caecal microorganisms have been described previously (Bakke, 1971). The substrate concentration was 0·5 mg ml^{-1} and aliquots of the incubates contained from 10 μg to 2 mg ml^{-1} of the decarboxylase inhibitor.

After anaerobic incubation of L-dopa with caecal microorganisms at 37° for 44 h, the formation of 3,4-dihydroxyphenylacetic acid, 3-hydroxyphenylacetic acid, 3-hydroxyphenylpropionic acid and 4-methylcatechol was demonstrated by t.l.c. None of these metabolites was found in the incubates containing Ro 4-4602 at a concentration of 1 mg ml^{-1} and partial inhibition was obvious with concentrations down to 0·1 mg ml^{-1}. These findings suggested that several steps in the microbial pathway could be inhibited by Ro 4-4602.

When 3,4-dihydroxyphenylacetic acid was used as a substrate, the amount of the *para* dehydroxylated metabolite 3-hydroxyphenylacetic acid was significantly reduced in the presence of 0·1 mg ml^{-1} of the inhibitor. Higher concentrations were required to affect decarboxylation to 4-methylcatechol.